SEARCH REQUEST FORM

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_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

✓ Other (CAN)

67293

STIC-Biotech/ChemLib

From: STIC-ILL
Sent: Thursday, May 23, 2002 12:13 PM
To: STIC-Biotech/ChemLib
Subject: RE: 09/784,005

10A03

-----Original Message-----
From: Meller, Michael
Sent: Thursday, May 23, 2002 12:12 PM
To: STIC-ILL
Subject: 09/784,005

Please search SEQ ID NO: 1 and return the results to me by email.

Thanks.

11B01

STIC-Biotech/ChemLib

From: Chan, Christina
Sent: Thursday, May 23, 2002 12:45 PM
To: Meller, Michael; STIC-Biotech/ChemLib
Subject: RE: 09/784,005

Point of Contact:
Beverly Shears
Technical Info. Specialist
CM1 1E05 Tel: 308-4994

Please rush. Thanks Chris

-----Original Message-----
From: Meller, Michael
Sent: Thursday, May 23, 2002 12:13 PM
To: Chan, Christina
Subject: FW: 09/784,005

Could you authorize a rush on this case since it was filed 2/16/2001.

Thanks

-----Original Message-----
From: Meller, Michael
Sent: Thursday, May 23, 2002 12:12 PM
To: STIC-ILL
Subject: 09/784,005

Please search SEQ ID NO: 1 and return the results to me by email.

Thanks.

Searcher: _____
Phone: _____
Location: _____
Date Picked Up: _____
Date Completed: _____
Searcher Prep/Review: _____
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TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST(where applic.)
STN: _____
DIALOG: _____
Questel/Orbit: _____
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Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: _____
Other (specify): _____

Meller
09/784005

FILE 'REGISTRY' ENTERED AT 13:35:44 ON 24 MAY 2002
L1 292 S DRVYIHPF/SQSP

(FILE 'CAPLUS' ENTERED AT 13:36:17 ON 24 MAY 2002)
L1 292 SEA FILE=REGISTRY ABB=ON PLU=ON DRVYIHPF/SQSP
L2 2338 SEA FILE=CAPLUS ABB=ON PLU=ON L1
L4 12 SEA FILE=CAPLUS ABB=ON PLU=ON L2(L)(?CANCER? OR ?TUMOUR? OR ?TUMOR? OR ?NEOPLAS? OR ?CARCIN?)

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:144752 CAPLUS
DOCUMENT NUMBER: 132:161695
TITLE: Cancer treatment with an angiotensin
INVENTOR(S): Vinson, Gavin Paul; Puddefoot, John Richard; Berry, Miles Gordon
PATENT ASSIGNEE(S): Queen Mary & Westfield College, UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010590	A2	20000302	WO 1999-GB2727	19990818
WO 2000010590	A3	20000518		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9954348	A1	20000314	AU 1999-54348	19990818
EP 1104305	A2	20010606	EP 1999-940353	19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
GB 1998-18023 A 19980818
GB 1998-20000 A 19980914
WO 1999-GB2727 W 19990818

AB A method of treatment or prevention of metastasis of cancer cells comprises administration of an effective amt. of an angiotensin to a patient. The use of an angiotensin in the prepn. of a medicament for the prevention of metastasis of cancer cells is also described. A second aspect of the invention is a method of inducing expression of .beta.1-integrin mols. in cancer cells to prevent or treat metastasis by administering an effective amt. of an angiotensin.

IT **4474-91-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cancer** metastasis treatment with angiotensin)

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:58041 CAPLUS

DOCUMENT NUMBER: 130:265628
TITLE: ACTH receptor mRNA in human adrenocortical tumors: overexpression in aldosteronomas
AUTHOR(S): Arnaldi, G.; Mancini, V.; Costantini, C.; Giovagnetti, M.; Petrelli, M.; Masini, A.; Bertagna, X.; Mantero, F.
CORPORATE SOURCE: Division of Endocrinology, Dept. of Internal Medicine, University of Ancona, Ancona, Italy
SOURCE: Endocrine Research (1998), 24(3 & 4), 845-849
CODEN: ENRSE8; ISSN: 0743-5800
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We previously reported that ACTH receptor (ACTH-R) mRNA is expressed in cortisol-secreting adrenal tumors, with significant differences between adenomas and carcinomas. In order to complete the study we have now evaluated 11 aldosteronomas (APA), 14 non-hypersecreting adenomas, 2 androgen-secreting adenomas and 8 normal adrenal glands. The level of ACTH-R mRNA was evaluated by competitive RT-PCR using a non-homologous competitor. ACTH-R gene was expressed in all tissues. All APA showed highest ACTH-R mRNA levels. Despite signs of individual heterogeneity, the level of ACTH-R transcripts was reduced in carcinomas. Furthermore, no significant differences were obsd. among cortisol-secreting adenomas, non hypersecreting adenomas and controls. The results show that ACTH-R mRNA is expressed in all adrenocortical tumors. The overexpression of ACTH-R in APA supports the role of ACTH on aldosterone secretion in these tumors, as also suggested by the presence of a diurnal rhythm, the lack of response to Angiotensin II, upright posture and captopril administration. The low abundance of ACTH-R in carcinomas might be a useful mol. marker of malignancy even if some overlap between carcinomas and adenomas does exist.
IT **4474-91-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ACTH receptor mRNA in human adrenocortical **tumors**)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:770513 CAPLUS
DOCUMENT NUMBER: 130:166393
TITLE: Angiotensin II receptors on colorectal carcinoma cells
AUTHOR(S): Kucerova, Dana; Zelezna, Blanka; Sloncova, Eva; Sovova, Vlasta
CORPORATE SOURCE: Institute of Molecular Genetics, Academy of Sciences of the Czech Republic, Prague, 166 37/6, Czech Rep.
SOURCE: International Journal of Molecular Medicine (1998), 2(5), 593-595
CODEN: IJMMFG; ISSN: 1107-3756
PUBLISHER: International Journal of Molecular Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The presence of angiotensin II receptors was found on cells of three colorectal carcinoma cell lines. The binding assays with

125I-labeled angiotensin II and ligands specific for angiotensin AT1 or AT2 receptors showed that angiotensin receptors on colorectal cancer cells are mostly of the AT2 type. The binding capacity of tumor cells was not significantly changed by butyrate-induced differentiation.

IT **4474-91-3**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(angiotensin AT1 and AT2 receptors in human colorectal **carcinoma** cells)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:312902 CAPLUS
DOCUMENT NUMBER: 129:52857
TITLE: Endothelin receptors and angiotensin II receptors in tumor tissue
AUTHOR(S): Kohzuki, M.; Tanda, S.; Hori, K.; Yoshida, K.; Kamimoto, M.; Wu, X. -M.; Sato, T.
CORPORATE SOURCE: Section of Internal Medicine and Disability Prevention, Tohoku University Graduate School of Medicine, Sendai, 980-77, Japan
SOURCE: Journal of Cardiovascular Pharmacology (1998), 31(Suppl. 1, Endothelin V), S531-S533
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In cancer chemotherapy, selective enhancement of drug delivery to tumor tissue is essentially important for increase of chemotherapeutic effects. An attenuated vasoconstrictive response to angiotensin II (Ang II) in tumors and a marked increase in tumor blood flow were obsd. compared with normal tissues during systemic hypertension induced by Ang II infusion. The phenomenon was absent when hypertension was provoked by endothelin-1 (ET-1). We assessed this response to characterize ET receptor and Ang II receptor d. and affinity in normal and tumor tissues. The tumor cell line LY80 was transplanted to the skin in nude rats. Four weeks later the rats were sacrificed. [125I] ET-1 and [125I Sar1, Ile8]-Ang II were used to map the receptors for ET and Ang II in rat tissues using computerized in vitro autoradiog. A moderately high d. of ET receptors, (ETB>ETA) was found in tumors. The Ang II receptors were markedly reduced in tumor tissues without changes in the affinity. These results suggest that the decrease in Ang II receptors but not ET receptors in tumors may explain the hemodynamic effect of Ang II-induced hypertension and ET-induced hypertension on tumor blood flow.

IT **4474-91-3**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endothelin receptors and angiotensin II receptors in **tumor** tissue in relation to **tumor** blood flow)

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:102133 CAPLUS
DOCUMENT NUMBER: 128:212591

TITLE: Reactivity of antineoplastic drugs with model peptides studied by advanced mass spectrometry methodologies

AUTHOR(S): Carbone, Virginia; Pocsfalvi, Gabriella; Sannolo, Nicola; Malorni, Antonio

CORPORATE SOURCE: International Mass Spectrometry Facilities Centre-National Research Council, Naples, 80131, Italy

SOURCE: NATO ASI Ser., Ser. C (1997), 504(Selected Topics in Mass Spectrometry in the Biomolecular Sciences), 413-425
CODEN: NSCSDW; ISSN: 0258-2023

PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vivo interaction of the antineoplastic drug 1-3-bis-(2-chloroethyl)-1-nitrosourea (BCNU) and acrolein with model peptides has been investigated to provide a detailed description of their electrophilic reactivity towards biol. macromols. Following incubation with these substances, the modified species were sepd. by HPLC and identified by fast atom bombardment mass spectrometry, whereas the reactive amino acids within the peptides structure were assigned by tandem mass spectrometry. Incubation with BCNU led essentially to the formation of an N-terminal carbamoyl-deriv. that slowly decompd. to form three isomeric structures and a very minor ethylated adduct. Alkylation with acrolein gives rise to a mixt. of different adducts due to the reaction of both the double bond and the carbonyl group. Two species contg. intramol. cross-links were also obsd. These results constitute the pre-requisite for in vitro and in vivo studies on the modification of Hb in patients following treatment with antineoplastic drugs.

IT **484-42-4**
RL: RCT (Reactant)
(mass spectrometric anal. of electrophilic reactivity of **antineoplastic** drugs with model peptide)

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:499236 CAPLUS
DOCUMENT NUMBER: 121:99236

TITLE: Disseminated intravascular coagulation observed following the effective chemotherapy for tumor sc transplanted in rats

AUTHOR(S): Li, Hao Chuan; Suzuki, Maroh; Khato, Juneji; Hori, Katsuyoshi; Saito, Sachiko; Tanda, Shigeru; Zhang, Qui Hang; Endo, Eiko; Ohta, Eiko

CORPORATE SOURCE: Inst. Dev., Aging Cancer, Tohoku Univ., Sendai, 980, Japan

SOURCE: Karei Igaku Kenkyusho Zasshi (1994), 45(3/4), 101-11
CODEN: KIKZEP

DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB A markedly effective treatment for cancer resulted frequently in a fatal outcome with disseminated intravascular coagulation (DIC). A new drug delivery system, flooding-the-castle chemotherapy (FCC) selectively enhances the drug concn. and its retention time in tumor tissues. This treatment caused marked effects of the anticancer drug on s.c. transplanted solid tumors, with resulting severe DIC.

An attack of DIC depended on the difference of tumor strains. Rats bearing AH272 tumor did not cause DIC even in complete cures following FCC. AH109A tumors, on the other hand, produced fatal DIC after a redn. in tumor size. However, even in rats bearing AH109A tumor, DIC did not occur when the efficacy of the drug was slight. These results suggest that DIC does not result from adverse reactions of FCC itself. Onset of DIC correlated well with changes of blood coagulability. However, there were no relations between DIC following chemotherapy and coagulation activities in tumor cells as well as in tissues of 2 tumor strains.

IT **4474-91-3**, Human angiotensin II
RL: BIOL (Biological study)
(flooding-the-castle **cancer** chemotherapy with mitomycin C and nitroprusside and, disseminated intravascular coagulation induced by)

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:46571 CAPLUS
DOCUMENT NUMBER: 120:46571
TITLE: Microvascular mechanisms of change in tumor blood flow due to angiotensin II, epinephrine, and methoxamine: A functional morphometric study
AUTHOR(S): Hori, Katsuyoshi; Zhang, Qiu Hang; Saito, Sachiko; Tanda, Shigeru; Li, Hao Chuan; Suzuki, Maroh
CORPORATE SOURCE: Dep. Tumor Microcircul., Tohoku Univ., Sendai, 980, Japan
SOURCE: Cancer Res. (1993), 53(22), 5528-34
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To elucidate the microvascular mechanisms of change in tumor blood flow elicited by vasopressors, a functional morphometric study of the s.c. microcirculation within a rat transparent chamber was performed. Arteriolar vessels were classified centripetally (a2.a5) according to Strahler's method. Arteriolar pressure in each segment both under normotension and under hypertension induced by angiotensin II, epinephrine, or methoxamine was measured using a microocclusion technique. Vasoconstriction was estd. by changes in vessel diams. In addn., tissue blood flow the subcutis and s.c. tumor (LV80, a variant of Yoshida sarcoma) under the same conditions was measured with the hydrogen clearance method. By comparing the sites of the greatest pressure drop and the vasoconstriction induced by each vasopressor, the authors assessed the sites of vascular resistance (VR) which showed increases due to these vasopressors. The greatest VR increase elicited by angiotensin II occurred across a2 vessels. On the other hand, the sites of VR increase due to epinephrine were in a3 vessels and larger vessels upstream from a3 arterioles. The VR increase induced by methoxamine was much smaller than that induced by epinephrine. The authors conclude that the fact that the sites of increased VR differ with each vasopressor is the primary reason that various vasopressors have been found to produce different changes in tumor blood flow.

IT **4474-91-3**, Human angiotensin II
RL: BIOL (Biological study)
(**tumor** blood flow response to, microvascular mechanism for)

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:24277 CAPLUS
DOCUMENT NUMBER: 120:24277
TITLE: Pharmacological manipulation of blood flow
AUTHOR(S): Hirst, Dvaid G.; Tozer, Gillian M.
CORPORATE SOURCE: Gray Lab., Mt. Vernon Hosp., Northwood/Middlesex, HA6 2JR, UK
SOURCE: BJR Suppl. (1992), 24(Radiation Science--of Molecules, Mice and Men), 118-22
CODEN: BJRSEF; ISSN: 0961-2653
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of angiotensin II on cardiac output distribution and abs. perfusion of rat and mouse tumors in relation to their host normal tissues were studied. In mice angiotensin II increased cardiac distribution to intradermal and gut wall tumors but decreased it to i.m. and adipose tumors. In rats bearing carcinosarcomas, angiotensin II had no effect on abs. perfusion of the heart and brain, but decreased the abs. perfusion of the tumor and produced even greater decreases in the abs. perfusion of the small intestine, muscle, kidney, and skin over the tumor. Thus, an angiotensin II infusion might be useful for enhancing the relative delivery of blood-borne agents to tumors compared with their host tissue in some cases.
IT **4474-91-3**, Angiotensin II
RL: BIOL (Biological study)
(circulation of **neoplasm** and host tissue response to)

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:551785 CAPLUS
DOCUMENT NUMBER: 119:151785
TITLE: Augmentation of tumor delivery of macromolecular drugs with reduced bone marrow delivery by elevating blood pressure
AUTHOR(S): Li, C. J.; Miyamoto, Y.; Kojima, Y.; Maeda, H.
CORPORATE SOURCE: Sch. Med., Kumamoto Univ., Kumamoto, 860, Japan
SOURCE: Br. J. Cancer (1993), 67(5), 975-80
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effects of angiotensin II (AT-II)-induced hypertension on the distribution of macromols. to Walker carcinoma and to bone marrow of SMANCS [poly(styrene-co-maleic acid)-neocarzinostatin conjugate] were investigated in rats. AT-II-induced hypertension from about 100 to 150 mmHg significantly increased the accumulation of the macromol. drug SMANCS and 51Cr-labeled bovine serum albumin ([51Cr]BSA), representatives of macromol. drugs, in tumor tissue. At 1 h after i.v. administration, intratumor concns. of [51Cr]BSA and SMANCS were elevated by 1.2-1.8-fold. The higher drug accumulation in the tumor that was produced by the artificial hypertension was retained even 6 h after administration. This observation indicates an additive effect to that under normotensive conditions where intratumor macromol. drug concns. increase steadily during this period. Furthermore, distributions of these drugs in the bone marrow and the small intestine decreased during artificial hypertension to 60-80% of those in the normotensive state. Therefore, the drug concn. ratios of tumor/bone marrow and tumor/small intestine were increased by 1.8-2.4-fold. A decreased

distribution of SMANCS to normal tissues under hypertensive conditions was also confirmed by the significant redn. of its toxicity e.g. leukopenia, diarrhea, and body wt. loss, even at a LD. On the contrary, [3H]methylglucose showed no remarkable difference in tumor or bone marrow accumulation under this hypertensive condition. These results show the advantages of macromols. over small mols. for AT-II-induced hypertension chemotherapy.

IT **4474-91-3**
RL: BIOL (Biological study)
(hypertension from, **antitumor** macromol. drug delivery enhancement by)

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:485560 CAPLUS
DOCUMENT NUMBER: 119:85560
TITLE: Analysis and distribution of etoposide in rat brain tumor model: intracarotid versus intracarotid with angiotensin II-induced hypertension
AUTHOR(S): Ogasawara, Hidenori; Uozumi, Tohru; Kiya, Katsuzo; Kurisu, Kaoru; Mikami, Takashi; Hotta, Takuhiro; Sugiyama, Kazuhiko
CORPORATE SOURCE: Sch. Med., Hiroshima Univ., Hiroshima, Japan
SOURCE: Cancer Invest. (1993), 11(3), 299-305
CODEN: CINVD7; ISSN: 0735-7907
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The brain tissue distribution of etoposide was investigated in 9L gliosarcoma-bearing rats with or without hypertension induced by angiotensin II (AT II). The rat brain tumor models were divided into the following 2 groups according to etoposide administration route: intracarotid injection (IC) group and intracarotid injection with hypertension induced by AT II (IHIC) group. Ten mg/kg of etoposide was given, and 30 min and 2, 4, 8, and 24 h later the rats were sacrificed. The drug concns. in the serum, tumor, and normal brain tissue were analyzed by HPLC. The etoposide concn. in the serum, tumor, and normal brain tissue peaked at 30 min in both groups. The serum concn. was similar between the 2 groups. The etoposide concn. in the tumor was at least 2.2 times higher in the IHIC group than in the IC group at 30 min and 2 h. The area under drug concn. curve (AUC) in the tumor in the IHIC group was about 2.2 times higher than that in the IC group. The etoposide concn. in the normal brain on the drug injection side changed only slightly from 0.5 h to 4 h and was about 3 times higher in the IHIC group than in the IC group. The etoposide concn. in the contralateral normal brain was very low in both groups at 30 min and disappeared thereafter. Intracarotid of anticancer drugs with AT II-induced hypertension further increases the drug concn. and AUC in the tumor compared with intracarotid injection alone and can be useful in treatment of malignant brain tumors.

IT **4474-91-3**
RL: BIOL (Biological study)
(hypertension induction by, in pharmacokinetic study of etoposide with brain **tumors**)

L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:98962 CAPLUS
DOCUMENT NUMBER: 116:98962

TITLE: Fluctuations in tumor blood flow under normotension and the effect of angiotensin II-induced hypertension

AUTHOR(S): Hori, Katsuyoshi; Suzuki, Maroh; Tanda, Shigeru; Saito, Sachiko; Shinozaki, Mika; Zhang, Qiu Hang

CORPORATE SOURCE: Res. Inst. Tuber. Cancer, Tohoku Univ., Sendai, 980, Japan

SOURCE: Jpn. J. Cancer Res. (1991), 82(11), 1309-16
CODEN: JJCREP; ISSN: 0910-5050

DOCUMENT TYPE: Journal
LANGUAGE: English

AB To elucidate the significance of angiotensin II (AII)-induced hypertension chemotherapy, changes of tissue blood flow both in normal subcutis and in tumors (AH109A, LY80) were measured in anesthetized rats with the hydrogen gas clearance method. Tissue blood flow in normal subcutis and tumors always fluctuated with time under normotension. The nature and the rate of fluctuation in tumor blood flow were almost identical in two different types of tumors. The fluctuation of blood flow in tumor and in normal subcutis were almost always inversely related when blood flows in their different tissues were measured simultaneously. When tissue blood flow in normal subcutis decreased, tumor blood flow increased, and vice versa. The connection mode between the tumor vascular bed and normal vascular bed maybe a parallel circuit. Vascular resistance in the normal vascular bed under AII-induced hypertension seemed to be greater than that under normotension, because the AII-increased tumor blood flow always exceeded the max. tumor blood flow under normotension. Due to the fluctuations of tumor blood flow, no-flow or low-flow areas resistant to delivery of anticancer drugs moved sporadically within the tumor under the normotensive condition. Good conditions for drug delivery to tumor tissues were induced by AII-induced hypertension.

IT **4474-91-3**
RL: BIOL (Biological study)
(hypertension from, **tumor** tissue circulation increase by, **antitumor** drug delivery in relation to)

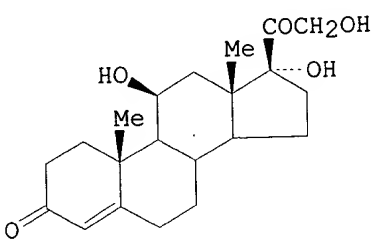
L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:569845 CAPLUS
DOCUMENT NUMBER: 99:169845
TITLE: Effects of angiotensin II and ACTH on normal and tumorous human adrenocortical cells

AUTHOR(S): Belmega, Wolfgang; Oelkers, Wolfgang; Belkien, Lutz; Shirpai, Monika; Fiedler, Ulrich; Haering, Rudolf

CORPORATE SOURCE: Klin. Steglitz, Freie Univ. Berlin, Berlin, Fed. Rep. Ger.

SOURCE: Acta Endocrinol. (Copenhagen) (1983), 104(1), 103-9
CODEN: ACENA7; ISSN: 0001-5598

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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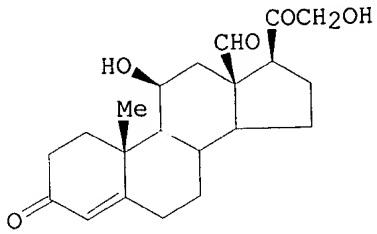

II

AB Isolated adrenocortical cells from 6 patients with a normal zona fasciculata, 4 patients with a normal zona glomerulosa, and **tumor** cells from 1 adrenocortical adenoma and 1 **carcinoma** were incubated with and without increasing concns. of ACTH 1-24 [16960-16-0] (10-13 to 10-9M) or Asp1-Ile5-angiotensin II [**4474-91-3**] (10-11 to 10-7M). In 4 of 5 normal cases, cortisol (I) [50-23-7] formation was clearly stimulated by 10-13M ACTH. The max. of the dose-response curve (5-fold stimulation) was reached at 10-10M ACTH. Angiotensin II (AII) started to stimulate normal cells at 10-11M, with a max. (2-fold stimulation) at 10-9M. Aldosterone (II) [52-39-1] prodn. by normal cells was less markedly stimulated by ACTH and AII, although the threshold doses for both peptides were similar to those of the cortisol response curves. The cells of the adrenocortical adenoma from a patient with Cushing's syndrome produced large amts. of cortisol and small amts. of aldosterone, both steroids being clearly stimulated by ACTH and AII. The adrenocortical **carcinoma** cells produced small amts. of cortisol and no aldosterone. Cortisol prodn. responded to ACTH, but not to AII. Apparently, an activated renin-angiotensin system may stimulate the zona fasciculata, since 10-11M AII (= 10 pg AII/mL) is a normal plasma AII concn. on an unrestricted diet. Clin. evidence supporting this thesis is reviewed. However, cortisol prodn. itself will rarely be increased by AII in vivo, since a down-regulation of ACTH would occur.

IT **4474-91-3**
RL: BIOL (Biological study)
(corticosteroids formation by normal and **neoplastic** human adrenocortical cells response to)

E39 THROUGH E40 ASSIGNED

FILE 'REGISTRY' ENTERED AT 13:41:05 ON 24 MAY 2002
L5 2 SEA FILE=REGISTRY ABB=ON PLU=ON (4474-91-3/BI OR 484-42-4/BI)

=> s l5 and l1
L6 2 L5 AND L1

L6 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN **4474-91-3** REGISTRY
CN Angiotensin II, 5-L-isoleucine- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Alanine, N-[1-[N-[N-[N-[N-(N2-L-.alpha.-aspartyl-L-arginyl)-L-valyl]-L-tyrosyl]-L-isoleucyl]-L-histidyl]-L-prolyl]-3-phenyl-, L- (6CI, 7CI)
OTHER NAMES:

CN 10: PN: WO0212471 SEQID: 17 unclaimed sequence
CN 1: PN: US6022696 SEQID: 2 unclaimed sequence
CN 1: PN: WO0002905 SEQID: 1 claimed protein
CN 1: PN: WO0056345 SEQID: 1 claimed sequence
CN 1: PN: WO0101138 SEQID: 1 claimed protein
CN 1: PN: WO0143761 SEQID: 1 claimed protein
CN 1: PN: WO0144270 SEQID: 1 unclaimed sequence
CN 1: PN: WO0155176 SEQID: 1 claimed protein
CN 1: PN: WO0198325 SEQID: 1 claimed protein
CN 2: PN: JP2001354699 PAGE: 2 unclaimed sequence
CN 2: PN: WO0168113 SEQID: 2 unclaimed sequence
CN 31: PN: WO0198325 SEQID: 32 claimed protein
CN 32: PN: WO0056345 SEQID: 32 claimed sequence
CN 36: PN: WO9958140 SEQID: 32 claimed protein
CN 3: PN: WO0224681 SEQID: 3 unclaimed sequence
CN 455: PN: WO0069900 SEQID: 641 unclaimed sequence
CN 4: PN: WO0101138 PAGE: 8 claimed protein
CN 5-Isoleucine-angiotensin II
CN 5-L-Isoleucineangiotensin II
CN 5: PN: WO0018899 PAGE: 18 unclaimed sequence
CN 80: PN: US6017693 TABLE: 4 claimed sequence
CN 8: PN: WO9958140 SEQID: 1 claimed protein
CN Angiotensin II (human)
CN Angiotensin II (mouse)
CN Human angiotensin II
CN Isoleucyl5-angiotensin II
CN L-Phenylalanine, N-[1-[N-[N-[N-[N-(N2-L-.alpha.-aspartyl-L-arginyl)-L-valyl]-L-tyrosyl]-L-isoleucyl]-L-histidyl]-L-prolyl]-
CI COM
SQL 8

SEQ 1 DRVYIHPF
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HITS AT: 1-8

REFERENCE 1: 136:323235

REFERENCE 2: 136:303787

REFERENCE 3: 136:289342

REFERENCE 4: 136:279477

REFERENCE 5: 136:276796

REFERENCE 6: 136:273519

REFERENCE 7: 136:261298

REFERENCE 8: 136:261054

REFERENCE 9: 136:257705

REFERENCE 10: 136:257409

L6 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN **484-42-4** REGISTRY
CN Angiotensin I, 5-L-isoleucine- (8CI, 9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Leucine, N-[N-[N-[1-[N-[N-[N-[N-(N2-.alpha.-aspartylarginyl)valyl]tyrosyl]isoleucyl]histidyl]prolyl]-3-phenylalanyl]histidyl]- (6CI)
CN Leucine, N-[N-[N-[1-[N-[N-[N-[N-(N2-L-.alpha.-aspartyl-L-arginyl)-L-valyl]-L-tyrosyl]-L-isoleucyl]-L-histidyl]-L-prolyl]-3-phenylalanyl]-L-histidyl]-, L- (7CI)
OTHER NAMES:
CN 14: PN: EP1092724 SEQID: 1 unclaimed sequence
CN 1: PN: JP2001354699 PAGE: 2 unclaimed sequence
CN 1: PN: WO0168113 SEQID: 1 unclaimed sequence
CN 34: PN: WO0144270 SEQID: 37 claimed protein
CN 35: PN: WO0143761 SEQID: 37 claimed protein
CN 35: PN: WO0155176 SEQID: 37 claimed protein
CN 36: PN: WO0002905 SEQID: 37 claimed protein
CN 36: PN: WO0198325 SEQID: 37 claimed protein
CN 37: PN: WO0056345 SEQID: 37 claimed sequence
CN 452: PN: WO0069900 SEQID: 637 unclaimed sequence
CN 5-Isoleucine-angiotensin I
CN 5-L-Isoleucine-angiotensin I
CN 5: PN: US6022696 SEQID: 6 unclaimed sequence
CN 5: PN: WO0018791 SEQID: 5 claimed protein
CN 8: PN: WO0212471 SEQID: 15 unclaimed sequence
CN Angiotensin I (Callithrix jacchus gene angt)
CN Angiotensin I (human)
CN Angiotensin I (mouse)
CN Angiotensin I (rat)
CN Angiotensin I 5-isoleucine
CN Human angiotensin I
CN L-Leucine, N-[N-[N-[1-[N-[N-[N-[N-(N2-L-.alpha.-aspartyl-L-arginyl)-L-valyl]-L-tyrosyl]-L-isoleucyl]-L-histidyl]-L-prolyl]-L-phenylalanyl]-L-histidyl]-
CN [Ile5]-Ang I
CN [Ile5]-Angiotensin I
CI COM
SQL 10

SEQ 1 DRVYIHPFHL
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HITS AT: 1-8

REFERENCE 1: 136:310143

REFERENCE 2: 136:257705

REFERENCE 3: 136:257409

REFERENCE 4: 136:179833

REFERENCE 5: 136:132739

REFERENCE 6: 136:112649

REFERENCE 7: 136:80273

REFERENCE 8: 136:68705

REFERENCE 9: 136:66621

REFERENCE 10: 136:48819

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